

# Diffusion Tensor Imaging of Heterotopia: Changes of Fractional Anisotropy during Radial Migration of Neurons

Seung-Koo Lee and Jinna Kim

Department of Radiology and Research Institute of Radiological Science, Yonsei University College of Medicine, Seoul, Korea.

Received: March 17, 2009

Revised: September 1, 2009

Accepted: September 2, 2009

Corresponding author: Dr. Seung-Koo Lee,  
Department of Radiology and Research  
Institute of Radiological Science,  
Yonsei University College of Medicine,  
250 Seongsan-ro, Seodaemun-gu,  
Seoul 120-752, Korea.  
Tel: 82-2-2228-2373, Fax: 82-2-393-3035  
E-mail: [slee@yuhs.ac](mailto:slee@yuhs.ac)

• The authors have no financial conflicts of interest.

**Purpose:** Diffusion tensor imaging provides better understanding of pathophysiology of congenital anomalies, involving central nervous system. This study was aimed to specify the pathogenetic mechanism of heterotopia, proved by diffusion tensor imaging, and establish new findings of heterotopia on fractional anisotropy maps. **Materials and Methods:** Diffusion-weighted imaging data from 11 patients (M : F = 7 : 4, aged from 1 to 22 years, mean = 12.3 years) who visited the epilepsy clinic and received a routine seizure protocol MRI exam were retrospectively analyzed. Fractional anisotropy (FA) maps were generated from diffusion tensor imaging of 11 patients with heterotopia. Regions of interests (ROI) were placed in cerebral cortex, heterotopic gray matter and deep gray matter, including putamen. ANOVA analysis was performed for comparison of different gray matter tissues. **Results:** Heterotopic gray matter showed signal intensities similar to normal gray matter on T1 and T2 weighted MRI. The measured FA of heterotopic gray matter was higher than that of cortical gray matter ( $0.236 \pm 0.011$  vs.  $0.169 \pm 0.015$ ,  $p < 0.01$ , one way ANOVA), and slightly lower than that of deep gray matter ( $0.236 \pm 0.011$  vs.  $0.259 \pm 0.016$ ,  $p < 0.01$ ). **Conclusion:** Increased FA of heterotopic gray matter suggests arrested neuron during radial migration and provides better understanding of neurodevelopment.

**Key Words:** Heterotopia, congenital malformation, magnetic resonance imaging

## INTRODUCTION

During the development of the brain cortex, a radial glial fiber system forms and primitive neurons migrate from the ependymal surface to the cortex in a 1-to-1 matching pattern. If the migration process is interrupted, heterotopic gray matter forms along the route of neuronal migration and can take an island-shaped nodular form or an aggregated band form.<sup>1,2</sup> Heterotopia is often a cause of intractable seizures and psychiatric disorders,<sup>3-5</sup> but it can sometimes be detected in asymptomatic patients. When it is localized in form and found to be an epileptogenic lesion, surgical resection is the treatment of choice, and precise localization is essential.

Diffusion tensor imaging (DTI) is a recently introduced MR technique that can show white matter integrity and the direction of fiber arrangement *in vivo*. Its clinical application is now increasing in frequency. White matter bundles have

© Copyright:

Yonsei University College of Medicine 2010

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

higher anisotropy than gray matter because of the arrangement of fibers and increased water diffusion along a specific axis. Heterotopic gray matter, the neurons arrested during migration, is likely to have significant anisotropy due to its developmental background.<sup>6</sup>

The purpose of this study was to assess the utility of DTI in the evaluation of heterotopia and to improve understanding of the pathophysiologic mechanism of anomalous neuronal migration.

## MATERIALS AND METHODS

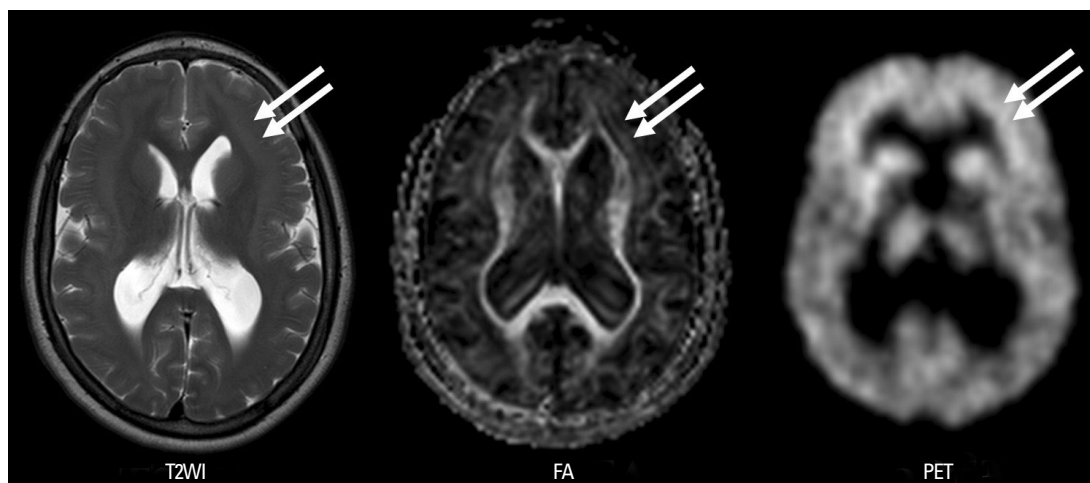
Diffusion-weighted imaging data from 11 patients (M : F = 7 : 4, aged from 1 to 22 years, mean = 12.3 years) who visited the epilepsy clinic and received a routine seizure protocol MRI exam and FDG-PET images were retrospectively analyzed. The exam included anatomical T2 weighted axial, FLAIR axial, oblique T2 weighted coronal, 3-D gradient echo T1 weighted coronal, and diffusion tensor imaging. MRI was performed using a 1.5T or 3.0T scanner (Achieva, Philips Medical Systems, Best, Netherlands) with an 8-channel Sensitivity Encoding (SENSE) head coil. DTI was performed using single-shot spin echo-echo planar imaging with SENSE factor 2. The imaging parameters were as follows: 220-mm field of view (FOV), 2 mm iso-voxel data acquisition with 2-mm slice thickness, TE = short as low as 48 ms at 3.0T and 70 ms at 1.5T scanner; TR = 6,599-8,280-ms according to slice number; number of signal acquisition = 2, b = 600 s/mm<sup>2</sup>, and 32-different diffusion gradient directions. The data were processed on a PC equipped with the Philips research imaging development environment (PRIDE) research software package (Philips Medical Systems, Best, Netherlands) or

operating console of MR scanner. Semi-quantitative analysis was performed for regions of interest (ROI) settled on heterotopic gray matter (HGM), and fractional anisotropy (FA) was measured. The FA of deep gray matter (DGM) from thalamus and cortical gray matter (CGM) were also measured. Cortical gray matter for the contralateral normal control was selected from slices showing heterotopic gray matter. Statistical analysis of DGM, HGM, and CGM was performed using ANOVA.

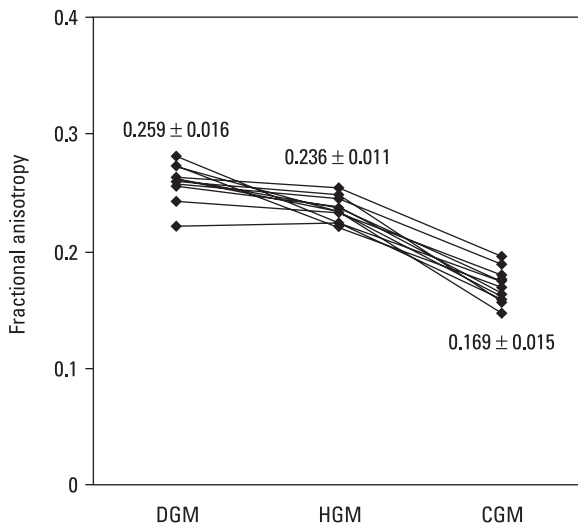
## RESULTS

Four patients had classical band heterotopia, i.e., a double-cortex with a linear gray-matter signal band in the white matter and intervening white matter between the heterotopia and normal cortex. Seven patients showed nodular heterotopia, including associated dysplastic cortex, and four of these had agenesis of the corpus callosum. For anatomical T2 weighted, FLAIR and 3-D gradient echo T1 weighted MRI, heterotopic gray matter showed the same signal intensity as the normal cortex. On FA maps, HGM showed higher signal intensity than that of the cerebral cortex or deep gray matter. Band-like high signal areas were noted on FA maps in the cases of band heterotopia (Fig. 1). All HGM showed a higher signal than that of CGM and a lower signal than those of DGM and normal white matter. On FDG-PET scan, heterotopic gray matter showed similar activity as cortical or deep gray matter, suggesting of high glucose metabolism as normal gray matter (Fig. 1).

On quantitative analysis, the FA of heterotopic gray matter was higher than that of cortical gray matter ( $0.236 \pm 0.011$  vs.  $0.169 \pm 0.015$ ,  $p < 0.01$ , one way ANOVA), and



**Fig. 1.** Twenty two year old male with intractable epilepsy. Note linear band of gray matter tissue with similar signal intensity as cortex and high FA values (double arrows). On PET scan, this heterotopic gray matter also shows high glucose metabolism than white matter (double arrows). FA, fractional anisotropy.



**Fig. 2.** Fractional anisotropy (FA) of gray matter tissues. Deep gray matter (DGM) is higher than heterotopic gray matter (HGM) and cortical gray matter (CGM). Note FA of HGM is also significantly higher than CGM.

slightly lower than that of deep gray matter ( $0.236 \pm 0.011$  vs.  $0.259 \pm 0.016$ ,  $p < 0.01$ ) (Fig. 2).

## DISCUSSION

Heterotopia is a type of cortical malformation in which the normal radial migration of neurons is arrested, causing gray matter tissue to be embedded in the white matter.<sup>2</sup> The etiology of heterotopia is unclear; some genetic factors have been reported,<sup>4,7</sup> while sporadic cases have also been described.<sup>8</sup> Prenatal infection is also known to be a factor causing the arrest of neuronal migration, resulting in the formation of heterotopic gray matter between the ependyma and cortex. Heterotopia has been divided into three groups based on clinical and imaging characteristics: subependymal, subcortical, and band heterotopia. On conventional MR imaging, heterotopic gray matter has signal intensity similar to that of normal gray matter and can appear nodular or curvilinear.<sup>9</sup> Functional MRI has revealed an activating signal at the heterotopic cortex,<sup>10-12</sup> and MR spectroscopy has shown efficacy in differentiating heterotopia from low-grade tumors.<sup>13</sup> Heterotopic neurons are considered mature since their metabolites are same as those of normal cortex.

Heterotopia has a wide range of clinical manifestations from asymptomatic to generalized tonic seizures.<sup>5</sup> A precise evaluation before surgery is critical because heterotopic gray matter is epileptogenic and can also affect major motor, vision, or sensory functions. MRI is the basic tool used to accomplish this.

During brain development, neurons migrate from the

ependymal surface to the cortex along the cytoarchitectural skeleton. Arrest during migration is the key pathology of heterotopia. Eriksson, et al.<sup>6</sup> reported increased fractional anisotropy of band heterotopia on DTI. They hypothesized that high anisotropy of ectopic gray matter was due to the nature of neuronal growth and partial volume averaging of the surrounding white matter. Previous histopathological study revealed that heterotopia consisted of unlayered small or medium sized rounded or pyramidal neurons, occasionally interrupted by small bundles of fibers.<sup>14</sup> Another study hypothesized that increased directivity of HGM indicated that the tissue was in the process of directional migration during neurodevelopment.<sup>15</sup>

In conclusion, this study suggests that increased anisotropy of heterotopic gray matter results from its histological nature and embryogenetic mechanism, i.e., gray matter tissue in white matter bundles and a radial growth pattern of neuronal migration. The results of this study will provide a better understanding of neuronal migration and the pathogenesis of ectopic gray matter during neurodevelopment.

## ACKNOWLEDGEMENTS

This study was supported by Yonsei University College of Medicine Faculty Fund #6-2007-0092.

## REFERENCES

- Livingston JH, Aicardi J. Unusual MRI appearance of diffuse subcortical heterotopia or "double cortex" in two children. *J Neurol Neurosurg Psychiatry* 1990;53:617-20.
- Gallucci M, Bozzao A, Curatolo P, Splendiani A, Cifani A, Passariello R. MR imaging of incomplete band heterotopia. *AJNR Am J Neuroradiol* 1991;12:701-2.
- Bourgeois JA, Nisenbaum J, Drexler KG, Dobbins KM, Hall MJ. A case of subcortical grey matter heterotopia presenting as bipolar disorder. *Compr Psychiatry* 1992;33:407-10.
- Kamuro K, Tenokuchi Y. Familial periventricular nodular heterotopia. *Brain Dev* 1993;15:237-41.
- Bauer J, Elger CE. Band heterotopia: a rare cause of generalized epileptic seizures. *Seizure* 1994;3:153-5.
- Eriksson SH, Symms MR, Rugg-Gunn FJ, Boulby PA, Wheeler-Kingshott CA, Barker GJ, et al. Exploring white matter tracts in band heterotopia using diffusion tractography. *Ann Neurol* 2002;52:327-34.
- Huttenlocher PR, Taravath S, Mojtahedi S. Periventricular heterotopia and epilepsy. *Neurology* 1994;44:51-5.
- Gleeson JG, Walsh CA. Neuronal migration disorders: from genetic diseases to developmental mechanisms. *Trends Neurosci* 2000;23:352-9.
- Barkovich AJ. Morphologic characteristics of subcortical heterotopia: MR imaging study. *AJNR Am J Neuroradiol* 2000;21:290-5.

10. Pinard J, Feydy A, Carlier R, Perez N, Pierot L, Burnod Y. Functional MRI in double cortex: functionality of heterotopia. *Neurology* 2000;54:1531-3.
11. Spreer J, Martin P, Greenlee MW, Wohlfarth R, Hammen A, Arnold SM, et al. Functional MRI in patients with band heterotopia. *Neuroimage* 2001;14:357-65.
12. Villani F, Vitali P, Scaioli V, Rodriguez G, Rosa M, Granata T, et al. Subcortical nodular heterotopia: a functional MRI and somatosensory evoked potentials study. *Neurol Sci* 2004;25:225-9.
13. Castillo M, Kwock L, Scatliff J, Gudeman S, Greenwood R. Proton MR spectroscopic characteristics of a presumed giant subcortical heterotopia. *AJNR Am J Neuroradiol* 1993;14:426-9.
14. Mai R, Tassi L, Cossu M, Francione S, Lo Russo G, Garbelli R, et al. A neuropathological, stereo-EEG, and MRI study of subcortical band heterotopia. *Neurology* 2003;60:1834-8.
15. Nucifora PG, Verma R, Lee SK, Melhem ER. Diffusion-tensor MR imaging and tractography: exploring brain microstructure and connectivity. *Radiology* 2007;245:367-84.